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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,915	10/23/2003	Anil Gulati	27611/38802A	6526

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,915	GULATI, ANIL	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *14-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Gulati, Anil

DETAILED ACTION

Election/Restrictions

The Election filed on April 11, 2005 and the supplemental Response filed on April 22, 2005 in response to the Restriction Requirement of March 8, 2005 has been entered. Applicant's election of Group I, claims 1-13, as specifically drawn to a method of treating a solid tumor comprising administering a therapeutically effective amount of an endothelin B agonist and a therapeutically effective amount of a second agent has been acknowledged. Furthermore, Applicant's election of IRL1620 as the specific endothelin B agonist has been acknowledged.

(Note: In the first election filed on April 11, 2005, Applicant elected BQ123 as the specific endothelin B agonist. The second election filed on April 22, 2005, Applicants pointed out that they erroneously elected BQ123 as the endothelin agonist and requested substitution of IRL1620 for BQ123 as the species. However, a review of the first election appears to suggest that BQ123 was elected NOT as a species, but as a distinct invention. Therefore, Applicant's election of IRL1620 will be interpreted as an election of an invention and NOT a species.)

Applicant's election with traverse of Group I, claims 1-13, and IRL1620 is acknowledged and has been entered. The traversal is on the grounds that the novelty of the invention is the use of an endothelin agonist in the treatment of a solid tumor, wherein the individual endothelin agonists are not independent and distinct inventions because the statutory requirements of 35 U.S.C. 121, namely, independence and distinctness are not present herein. For example, Applicants contend that the individual endothelin agonist are not independent inventions because the endothelin agonists set forth in the claims are so closely related that a search for applicants' elected endothelin agonist would necessarily encompass a search for the remaining endothelin agonists. Thus, Applicants submit that there is no evidence that a search and examination directed to endothelin agonist in general would be a *serious burden on the examiner*, as is required by MPEP 803. These arguments have been considered but are not found persuasive for the reasons set forth in the previous office action (03/08/2005) and for the reasons set forth below.

First, the MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Thus, while Applicants contend that the individual endothelin agonists are not independent or distinct invention because they are closely related, Applicant's have not provided evidence which suggests how these different agonist are related. For example, it appears from the terminology "endothelin B agonist" that the "compounds" function in a similar manner. However, there does not appear to be any chemical/structural features which are common to the instantly claimed agonist. As to the question of burden of search, a literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-43 are pending.

Claims 14-43 have been withdrawn from consideration as being drawn to non-elected inventions.

Claims 1-13 are currently under consideration.

Species Election

The Election filed on April 11, 2005 and the supplemental Response filed on April 22, 2005 in response to the Restriction Requirement of March 8, 2005 has been entered. Applicant's election with traverse of a breast tumor as the tumor, and paclitaxel as the chemotherapeutic has been acknowledged. With respect to the election of a single tumor, Applicants submit that these tumors are sufficiently related such that there would not be a serious burden, to encompass solid tumors in general. With regards to the election of a single chemotherapeutic, Applicants contend that the election of a single chemotherapeutic is unduly restrictive, wherein the administration of an endothelin agonist potentiates the chemotherapeutic effect, and this effect is independent of the chemotherapeutic agent. These arguments have been considered and are found to be partially persuasive for the reasons set forth below.

After careful review and reconsideration, the species election pertaining to the individual solid tumor has been withdrawn. With regards to the species election pertaining to a chemotherapeutic, Applicants have not provided any evidence which would suggest that the election

of a single chemotherapeutic agent is unduly restrictive. For example, Applicants contention that the endothelin agonist potentiates the chemotherapeutic effect which is independent of the chemotherapeutic agent is not pertinent because this does not appear to address how the chemotherapeutics are related. For example, the prior restriction requirement (page 5) stated that claim 6 is "generic to plurality of disclosed patentably distinct species comprising the following chemotherapeutic agents; adriamycin, camptothecin, carboplatin, ... topotecan which differ at least in chemical structure and mechanism of action such that one species could not be interchanged with the other. As such, each species would require different searches and the considerations of different patentability issues." Therefore, the species requirement pertaining to the chemotherapeutic agent is deemed proper and therefore made FINAL.

Information Disclosure Statement

The Information Disclosure Statements filed on 3/22/2004, 6/01/2004, 11/05/2004 and 11/24/2004 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Furthermore, the listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claim 4 is objected to because of the following informalities: Claim 4 is objected for being drawn to non-elected inventions such as ET-1, ET-2, ET-3, BQ3020, sarafotoxin 56c, [$Ala^{1,3,11,15}$]ET-1 . Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-5 are rejected as vague and indefinite for reciting the term IRL1620 in association with being an endothelin B agonist as the sole means of identifying the claimed molecule. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify IRL1620, for example, by chemical name and/or structure of IRL1620.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Patterson et al. (IDS, WO 01/00198, 2001).

In the instant case, the claims are drawn to a method of treating a solid tumor comprising administering to a mammal in need thereof a therapeutically effective amount of an endothelin B agonist and a therapeutically effective amount of a chemotherapeutic agent, wherein the endothelin B agonist is IRL1620. The solid tumor is further selected from ovarian, colon, Kaposi's sarcoma, a breast tumor, a melanoma, a prostate tumor, a meningioma, a liver tumor, and a breast phyllode tumor. The mammal is further drawn to a human.

Patterson et al. (page 2, line 27 to page 3, line 3 and page 6, lines 13-15) discloses a method of treating cancer, i.e. solid tumors, comprising administering to an individual in need thereof a therapeutically effective amount of an endothelin B an inhibitor of an endothelin B-receptor activity. With regards to the endothelin B inhibitor, the WO document teaches (page 8, lines 16-20) that the endothelin inhibitor includes but is not limited to IRL1620. With regards to the cancer, Patterson et al. teaches (page 6, lines 13-28) that cancer includes but is not limited to ovarian, colon, Kaposi's sarcoma, a breast tumor, a melanoma, a prostate tumor, a meningioma and a liver tumor. With regards to the individual, the WO document teaches (page 7, line 4) that the individual is generally a human subject. Patterson et al further teach (page 23, lines 17-19) that the compositions may be administered in conjunction with other compositions for the treatment, including but not limited to chemotherapeutics. Thus, while Patterson et al. describes IRL1620 as an inhibitor of endothelium activity and not an "endothelium agonist", the claimed method of using IRL1620 for the treatment of a solid tumor appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Moreover, even though the claims are drawn to a mechanism by which IRL1620 interacts with the endothelin B receptor, the claimed method does not appear to distinguish over the prior art teaching of the same or nearly the same method. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patterson et al. (IDS, WO 01/00198, 2001) in combination with Rowinsky et al. (N. Engl. J. Med. 1995; 332: 1004-1014).

Patterson *et al* teaches, as applied to claims 1-5 and 13 above, a method of treating a solid tumor comprising administering to a human in need thereof a therapeutically effective amount of IRL1620 and a therapeutically effective amount of a chemotherapeutic agent.

Patterson *et al.* does not teach that the chemotherapeutic agent is paclitaxel.

Rowinsky *et al.* discloses (page 1008, 2nd column to page 1011, 2nd column) paclitaxel and its importance as a chemotherapeutic agent in the treatment of a variety of cancer including but not limited to ovarian cancer, breast cancer, and lung cancer.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references in order to treat a cancer patient because each of the therapeutics had been individually taught in the prior art to be successful at treating cancer. The instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant method claims, one of ordinary skill in the art would have a reasonable expectation of success that the combination of IRL1620 as taught by Patterson et al and paclitaxel as taught by Rowinsky et al. could be used in a method for treating a solid tumor. Moreover, the strongest rationale for combining references is a recognition, expressly or impliedly in

the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983).

Claims 1-5 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patterson et al. (IDS, WO 01/00198, 2001).

Patterson *et al* teaches, as applied to claims 1-5 and 13 above, a method of treating a solid tumor comprising administering to a human in need thereof a therapeutically effective amount of IRL1620 in conjunction with therapeutically effective amount of a chemotherapeutic agent.

Patterson *et al.* does not teach that the endothelin B agonist and chemotherapeutic agent are administered simultaneously, as a single composition, as a separate composition or sequentially, wherein the chemotherapeutic agent is administered prior to or after the endothelin B agonist.

However, changes in the sequence of which ingredients are added would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. The instant situation is amenable to the type of analysis set forth in In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) where the court held that the selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results. See also In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is *prima facie* obvious.). Thus, the claimed variations in Applicants' process with respect to "time" of administration would have been obvious at the time of Applicants' invention, wherein the optimization of time of administration being well within the capabilities of the artisan of ordinary skill at the time of Applicants' invention.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
6/7/05